Journal of Harbin Engineering University
ISSN: 1006-7043
Vol 44 No. 8
August 2023

The Transformative Potential of Digital Twin Technology in Empowering Drug Discovery, Development, and Manufacturing with in the Metaverse

Avinash.C
Research Scholar, VELS Univesity Chennai,Tamil Nadu, India
Dr. B. Booba
Professor VELS University, Chennai, Tamil Nadu, India

Abstract: The transformative potential of digital twin technology within the metaverse for revolutionizing the pharmaceutical industry. Digital twins, virtual replicas of real-world entities, can be used in drug discovery, development, and manufacturing processes to unlock unprecedented insights and efficiencies.
In drug discovery, virtual testing of potential compounds within the metaverse accelerates the identification of promising candidates while reducing the need for costly physical experiments. Simulating molecule behavior enables accurate predictions of drug efficacy, toxicity, and side effects, speeding up the development of safe and effective medications.
Digital twins also facilitate advanced modeling of complex biological systems, aiding researchers in understanding disease mechanisms, drug targets, and personalized medicine. Tailored therapies can be designed for individual patients, leading to improved treatments and outcomes.
In pharmaceutical manufacturing, digital twins offer real-time monitoring and optimization of production processes, reducing waste and enhancing productivity. Predictive maintenance minimizes downtime and ensures uninterrupted production.
The integration of digital twin technology with the metaverse presents a paradigm shift, offering efficiencies, cost savings, and innovation. However, challenges related to data integration, security, and standardization must be addressed through collaboration among stakeholders.
Overall, the adoption of digital twin technology in the metaverse promises to revolutionize drug discovery, development, and manufacturing, ushering in a new era of progress in the pharmaceutical sector.
Keyword: Cognitive computing, Metaverse, Digital twin technology, Digital twin technol, Real-time monitoring, Deep learning, Artificial intelligence, Block Chain.

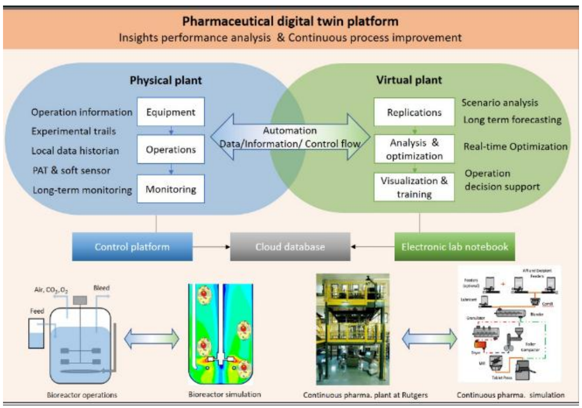

Fig1. Graphical Abstract

1. Introduction

The concept of a digital twin is somewhat self-explanatory: it is a virtual, digital copy. That copy can be of many things, though — a physical object, such as a product; a process, such as a manufacturing process; a system, such as a manufacturing facility; a network, such as a supply chain; or infrastructure, such as a city.[1,2]Digital twins are also more than digital copies; they are connected to their real-world counterparts from which real-time data (e.g., enterprise, Internet-of-Things (IoT)) are gathered and generated results are returned. The real world is simulated in the virtual environment using these data to predict possible performance outcomes and evaluate what-if scenarios. Using digital twins can help companies better understand their products, processes, and systems to facilitate better decision making and enable avoidance of future problems.
NASA developed the first digital twins in the 1960s, making copies of its spacecraft to perform simulations and train astronauts.[1] These digital twins played a key role in saving the lives of the astronauts on the problem-plagued Apollo 13 mission. By the 1970s, mainframe computers were

used to support basic digital twins of large facilities. In the 1980s, 2D computer-aided design (CAD) systems were used to provide technical drawings digitally and further build out initial digital twin solutions. The next decade brought 3D CAD with parametric modeling and simulation, and the following decade saw these systems cloud-connected for collaboration and program management.

Today, real-time 3D digital twins are developed using not only many different physical models and the IoT but artificial intelligence (AI), machine learning (ML), natural language processing, the "metaverse," and virtual and augmented reality (VR/AR).[3] For companies with the appropriate level of digital maturity, strong data infrastructures, experts with the right skills, and the ability and willingness to invest upfront in this new technology, they are improving performance in many industries and various applications. [2] Not only have improvements in digital technologies had an impact; automation systems and real-time analytical tools are providing the reliable and robust data needed to maximize the use of digital twins.

Digital twins provide an in silico means for optimizing products, processes, and systems at a much lower cost than what is required to perform physical experiments. [1–3] They also help reduce waste by predicting optimum maintenance scheduled and preventing problems. They are being used for many applications,[3] including the modeling of Los Angeles' transportation infrastructure and the entire city of Shanghai, China. A digital twin of Sofi Stadium in Los Angeles models the stadium and 300 surrounding acres. Tesla creates digital twins of all cars it produces to minimize the service and maintenance required.

Many Possible Applications for Digital Twins in Pharma Within the pharmaceutical industry, numerous potential applications for digital twins exist.[4,5] Perhaps one of the most obvious is the use of digital twins of manufacturing processes to increase efficiency and productivity by facilitating process optimization and scalability, as well as enabling predictive maintenance. There are less obvious uses as well. Digital twins of cells are determining if surgery is needed in heart patients and accelerating drug discovery, while drug development could be improved from a cost and time perspective through the use of digital twins as replacements for the placebo-control arms of clinical trials. Digital twins of diseases could help researchers better understand disease mechanisms and the impacts of drugs on disease progression, while digital twins of organs, genomes, and patients could better enable precision/personalized medicines. Digital twins of hospitals and clinics, meanwhile, could potentially improve patient care.

2. Overview Of Metaverse-Enabled Systems

Accelerating Drug Discovery with Cellular Digital Twins

Access to many types of omics data and sequencing information at the single-cell level combined with ML, particularly deep learning, and AI is enabling the development of digital twins of human cells for use in drug discovery. DeepLife is one company with a cellular digital twin platform based on single-cell omics data that it hopes will accelerate and optimize target identification. The cloud-based system can rapidly evaluate how different cells (up to 10 million) respond to billions of drugs and drug combinations, viruses, and other perturbations. In addition to discovery of novel drugs, it is also finding use in the repurposing/repositioning of existing drug substances/products.

2.1 Improving Clinical Trials with Digital Twin Technology

Clinical trials account for the largest portion of drug development costs and generally are inefficient. They typically also do not represent the true patient population or real-life experiences of patients. The use of placebos also means that a portion of patients is denied treatment. Digital twins can help overcome these issues by simulating diverse patient characteristics, accelerating patient selection, and predicting patient responses to allow elimination of placebo control arms.[7] They can also reduce the number of actual patients subjected to rea-world testing, increasing the efficiency, effectiveness, and safety of clinical trials while reducing their cost. That would enable more companies to run more trials and bring more needed medicines to market.

Another approach to addressing drug development challenges is the development of digital twins of human patients, organs, or cell receptors. Metaverse technologies are being deployed to provide immersive or AR visual representations of the effects of proposed therapies on these digital twins.

2.2 Benefits of Digital Twins in Pharma Manufacturing

A huge challenge in the pharmaceutical industry is the development of optimum robust and scalable processes from the outset. Doing so is imperative, however, to ensure cost-effective and reliable production of drug substances and drug products. Furthermore, making changes to approved processes involves the performance of extensive bridging studies — a lengthy and costly enterprise.

Digital twins have the potential to aid in the development of optimum processes that are robust, scalable, and commercialize.[9]. Most pharma companies already use computational fluid dynamics (CFD) software to model momentum, energy, and mass transport within reactors and bioreactors. Digital twins go a step further, incorporating CFD data with other information to predict optimal reactor designs, process parameters, and addition protocols. They can also be used to predict performance, thereby reducing the number of process performance qualification (PPQ) runs needed to establish robust control strategies, which can save millions of dollars.

Other benefits include more efficiently tracking processes to ensure compliance with regulatory requirements, improving data integrity, facilitation of the move to continuous processing, and reduced infrastructure costs.[10]Digital twins can also be used to track maintenance and operational issues to identify equipment that must be repaired or replaced before it fails and reduce the need for skilled labor, which is in short supply within the entire biopharma industry today.[11] Modeling using digital twins overall provides greater process understanding, which enables the development of more effective process control strategies and ultimately more robust processes.[12] McKinsey estimates the savings for pharma companies that leverage digital twins could experience increases in productivity of as much as 150–200%.11

Models used in digital twins of pharmaceutical manufacturing processes can be based on mathematical or stochastic models (or a combination of the two) that are integrated with geometric modelling techniques.[13] Currently used scale-down, physical models do not provide higher levels of process understanding and therefore have limited use.[12] Mechanistic models used to develop digital twins, on the other hand, include assumptions based on known principles as well as data, providing a more comprehensive description of the process and thus improved predictive power. Such holistic models, which generally leverage AI and real-time data, can help identify bottlenecks and lead to improvements across entire processes and plants.

Successful pharma manufacturing digital twins have both physical and virtual (ideally comprehensive, but typically simplified) components that communicate with one another with the goal of enabling the U.S. FDA's vision to develop a maximally efficient, agile, flexible pharmaceutical manufacturing sector that reliably produces high-quality drugs without extensive regulatory oversight.

[14]The physical component serves as the source of data, including critical process parameters (CPPs) for the equipment and process and critical quality attributes of the product, values of which are monitored using process analytical technology (PAT).

Virtual components perform real-time process simulations and system analyses, the results of which are sent to a data management platform for visualization and used to create control commands that are delivered to the physical process to ensure optimal control and performance.[14] Modeling platforms include MATLAB and Simulink (MathWorks), COMSOL Multiphysics (COMSOL),gPROMS FormulatedProducts (Process Systems Enterprise/Siemens), aspenONE products (AspenTech), and STAR-CCM+ (Siemens), among others. Cloud-based, IoT, software-as-a-service data management platforms include Predix (General Electric), Mindsphere (Siemens), SEEQ, TrendMiner, TIBCO Cloud, and others.

2.3 Commitment Required to Overcome Hurdles to Digital Twin Use in Pharma

To be maximally effective, digital twins require accurate data. In many pharmaceutical industry applications, those data may be sensitive, personal patient data — particularly for digital twins focused on supporting personalized medicines.4 Ensuring data security is therefore essential. Hesitancy surrounding AI applications and their use of personal data make this challenge more complicated.[7] One possible solution is to leverage another advanced solution — blockchain technology — to secure data.4

Digital twins for the pharma industry must also be created using a hodge-podge of data sources ranging from genomics information to cell culture process parameters and physician notes, creating the need for solutions that can manage disparate data types and forms.[7]

Beyond data integrity issues, regulatory acceptance and the general willingness to adopt digital twins may be additional concerns.[7] Successes are most likely to occur where digital twins represent continued advances in modeling, namely for pharma manufacturing. The concepts of digital twins for cells, organs, and patients and their use in clinical trials will be more slowly recognized.

Other larger issues relate to the upfront investment required to create digital twins and the time required before benefits can be realized.[13] Firms seeking to implement digital twins must not only be prepared for the effort and commitment required, but also have sufficient digital maturity and access to large quantities of appropriate, reliable and robust data, such as through the use of state-of-the-art PAT solutions for upstream and downstream processing.

GSK worked with French IT firm Atos and the engineering company Siemens to pilot a digital twin of one of its vaccine manufacturing processes, specifically a process for the production of a particular vaccine adjuvant.[15] The digital twin is connected to the real-world manufacturing process, allowing physical sensors to send data to the twin and the twin to provide simulated insights to the control system of the physical process. GSK is able to fine-tune the process in real time using a range of models and ML techniques, and as importantly identify and eliminate or control manufacturing variabilities, reducing risk and facilitating tech transfer. Based on the successes achieved during the pilot, the company expects to leverage digital twins for other vaccine manufacturing processes, potentially as simulators for operator training and ultimately see them used as routine tools.

Sanofi, meanwhile, is also exploring the use of digital twins for vaccine manufacturing.16 In its case, the goal is to establish optimal processes before actual deployment. For its software partner, the company turned to Dassault Systèmes and its simulated 3D spaces, a platform that Sanofi is using to create virtual manufacturing systems that mimic processes Sanofi has under development.

2.4 ChatGPT

Digital twins have emerged as a powerful concept with diverse applications in various industries, including the pharmaceutical industry. A digital twin is a virtual, digital copy of a physical object, process, system, or infrastructure that is connected to its real-world counterpart, gathering real-time data and generating predictive insights. The use of digital twins enables companies to better understand their products, processes, and systems, leading to improved decision-making and problem avoidance.

The origins of digital twins can be traced back to NASA in the 1960s when they developed virtual replicas of spacecraft to perform simulations and train astronauts. Over the years, advancements in technology, such as mainframe computers, CAD systems, and cloud connectivity, have contributed to the evolution of digital twins. Today, real-time 3D digital twins incorporate technologies like AI, machine learning, natural language processing, the "metaverse," and virtual and augmented reality.

In the pharmaceutical industry, digital twins have numerous potential applications. One of the obvious uses is in manufacturing processes, where digital twins can optimize efficiency, scalability, and predictive maintenance. They can also be used to create digital twins of cells, diseases, organs, genomes, patients, hospitals, and clinics, leading to advancements in areas such as surgery, drug discovery, personalized medicine, disease understanding, and patient care.

For drug discovery, digital twins of human cells based on omics data and deep learning algorithms can accelerate and optimize target identification and drug response evaluation. In clinical trials, digital twins can simulate diverse patient characteristics, predict patient responses, and eliminate the need for placebo control arms, leading to more efficient, effective, and cost-effective trials. Digital twins of pharmaceutical manufacturing processes offer benefits such as process optimization, reduced bridging studies, compliance tracking, data integrity improvement, and support for continuous processing.

However, there are challenges to overcome for the widespread adoption of digital twins in the pharmaceutical industry. Data security, especially when dealing with sensitive patient information, is a major concern. Blockchain technology can be leveraged to address this issue. Integration of disparate data types and forms is another challenge, requiring solutions that can manage diverse data sources effectively. Regulatory acceptance and the upfront investment required for digital twins are also important considerations.

Despite these challenges, pharmaceutical manufacturers are exploring the use of digital twins. Companies like GlaxoSmithKline (GSK) and Sanofi have conducted pilot studies to implement digital twins in their vaccine manufacturing processes. GSK, in collaboration with Atos and Siemens, has developed a digital twin that provides real-time insights and control over the manufacturing process, reducing variabilities and improving risk management. Sanofi is using Dassault Systemes simulated 3D spaces to create virtual manufacturing systems for optimal process development.

As the technology matures and pilot studies demonstrate their value, digital twins are expected to become more prevalent in the pharmaceutical industry, offering significant benefits in terms of productivity, efficiency, cost reduction, and quality improvement.

2.5 Digital Twin and Metaverse in Pharma:

A digital twin is a virtual representation of a physical object, system, or process. In the pharmaceutical industry, digital twins is used to model and simulate drug development processes, clinical trials, and manufacturing operations.

a. Drug Discovery and Development: Digital twins are used to simulate and optimize the design of drug molecules, predict their behavior in the human body, and accelerate the discovery and development process. This help in reducing costs and time required for bringing new drugs to market.

b. Personalized Medicine: Digital twins are created for individual patients by integrating their medical data, genetic information, and physiological parameters. These virtual models help in predicting drug responses and optimizing treatment plans for personalized medicine.

c. Manufacturing Optimization: Digital twins simulate and optimize pharmaceutical manufacturing processes, including equipment performance, supply chain logistics, and quality control. This led to improved efficiency, reduced downtime, and better product quality.

d. Clinical Trials: Digital twins simulate clinical trial scenarios, predict patient responses to treatments, and optimize trial protocols. This help in designing more efficient and cost-effective clinical trials, ultimately speeding up the development of new therapies.

2.6 Metaverse in Pharma:

The metaverse refers to a virtual shared space where users interact with each other and digital objects in real-time. In the pharmaceutical industry, the metaverse can have several applications:

a. Medical Education and Training: The metaverse provide immersive environments for medical students and professionals to learn and practice various medical procedures and techniques. It simulates complex surgeries, patient interactions, and medical emergencies.

b. Remote Collaboration: The metaverse enable global collaboration among researchers, scientists, and healthcare professionals. They interact, share data, and collaborate on research projects in a virtual environment, regardless of their physical location.

c. Patient Engagement and Education: Pharma companies leverage the metaverse to create interactive patient education platforms, virtual support groups, and immersive experiences to educate patients about diseases, treatments, and medication adherence.

d. Virtual Conferences and Events: The metaverse be used to host virtual conferences, scientific meetings, and healthcare events. Participants attend from anywhere in the world, interact with speakers, and explore virtual exhibits.

3. Methodology

A General Design Schema with a Specific Example of a Digital Twin for Drug Discovery, Testing and Repurposing

Schematic Program for developing a Medical Digital Twin. This provides a guide to a series of decisions that should be made when embarking on the development of Medical Digital Twin. An example of a specific use case for drug development, testing and repurposing can be seen in

Example Use Case: Development of Medical Digital Twins for Drug Development, Testing and Repurposing Section.

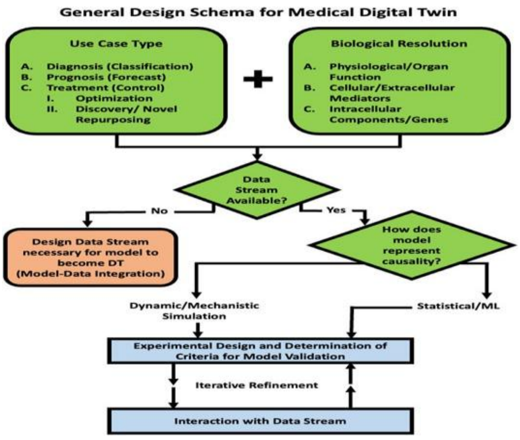

Figure 3.1. To specific requirements for the task of discovering and evaluating

The Drug Development Digital Twin (DDDT). We adapt the general schema in Figure 3.1 to specific requirements for the task of discovering and evaluating novel therapeutic agents and/or novel applications of existing drugs in novel contexts.

The unifying aspect of these tasks is that no prior clinical data exists because the interventions have not yet been tried. This results in the choices reflected by the Yellow Highlighted sections in the presented schema (compare to Figure 3.1 and see Text for details).

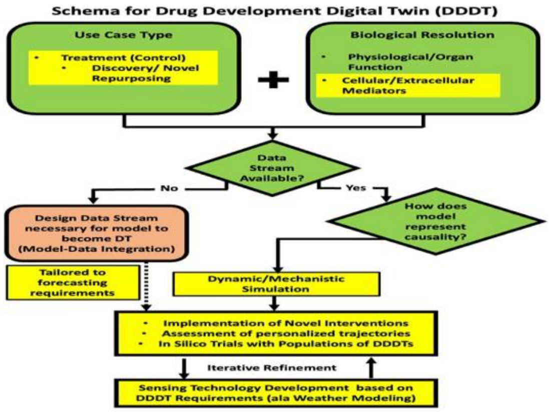

Figure 3.2 schematic program for developing a medical digital twin for drug discovery, testing and repurposing, the Drug Development Digital Twin (DDDT).

4. Open Challenges To The Metaverse Implementation In Healthcare

4.1 Leveraging Digital Twin For Pharma

Pharmaceutical companies face various challenges, including rising costs, expiring patents, declining profit margins, and stricter regulations. To address these issues, they are turning to digital twin technology, which allows them to simulate and visualize drug manufacturing processes in real-time. By leveraging digital twins, process engineers can predict process parameter variations, trigger alerts, and take corrective actions, leading to improved performance and operational efficiencies.

Infosys, a technology company, is actively working to build sustainable models of digital twins for pharmaceutical companies, aiming to drive digitization and cost reduction. They have collaborated with a global pharmaceutical client based in Europe to optimize the cell culture process in their vaccine development plant. The client sought better data visualization for bioreactors, remote process monitoring, and an educational gamification app for plant personnel training.

4.2 Digital Twin Architecture

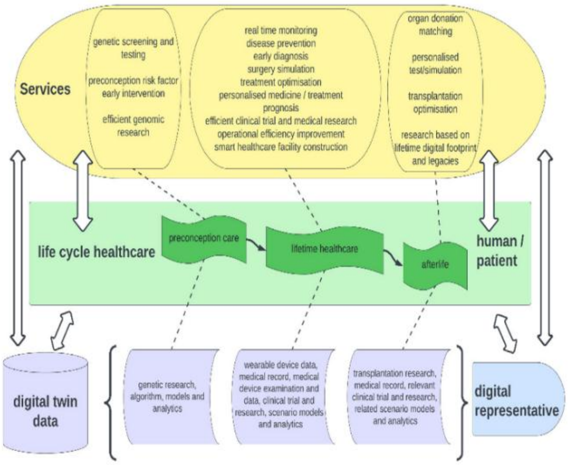

Figure 4.2 Digital Twin Architecture

1. Comprehend : The goals the organization wants to achieve by using the concept of Digital Twin.

2.Collate data points: Required to digitally replicate the physical systems and surroundings.

3. Enable easy access to data findings via mobile devices.

4 Infuse technologies: VR for better visualization of data and immersive, engaging user experience.

5 Include advancements: In predictive analytics to train systems to better forecast production and maintenance schedules.

4.3 Challenges:

1. Digital Divide: The concern that not everyone may have equal access to digital twin technologies, potentially leaving certain groups at a disadvantage in terms of healthcare services and benefits.

2. Access, Privacy, Ethics, and Security: As AI and digital twin technologies advance, there are concerns about ensuring equal access to these technologies while safeguarding patient privacy and maintaining ethical standards. Cybersecurity also becomes a crucial issue when dealing with sensitive healthcare data.

3. Suitability for Diverse Needs: Digital twin technologies should be designed to accommodate the diverse needs of patients and healthcare providers to ensure that the benefits are widely applicable.

4. Compatibility and Integration: Ensuring that digital twin platforms and systems are compatible with existing IT infrastructure and future technologies is essential for seamless integration and effective utilization in healthcare settings.

5.Standardization and Legislation: Establishing forward-thinking, unified standards and legislation for digital twin technologies is critical for sustainable development. This will prevent conflicting interests and prioritize long-term benefits over short-term profits.

6. Public Expectations and Realization: Early stages of technological development can generate inflated public expectations. It is crucial to manage these expectations and avoid misunderstandings and reputational damage.

7. Resource Allocation: If the expectations of digital twin technologies in healthcare are not met, there might be a negative impact on resource allocation for future long-term development.

4.4 Conclusions The research described aims to bridge the gap between digital twin technology and healthcare, providing insights for future development. It proposes a digital twin model in the healthcare context across different life stages, potentially extending digital twinning to all aspects of healthcare services. The research also emphasizes the need to consider healthcare aspects that are currently overlooked but could benefit from integrating digital twin technologies. Overall, while digital twin technologies offer enhanced value and benefits in healthcare, careful consideration and planning are essential to address the challenges and ensure equitable, secure, and ethical implementation for the benefit of all stakeholders involved.

References:

[1] "What is a digital twin?" Unity. Accessed 15 Feb. 2023.

[2] Borden, Kimberly and Anna Herlt. "Digital Twins: What could they do for your business." McKinsey Insights. 3 Oct. 2022.

[3] Marr, Bernard. "The Best Examples Of Digital Twins Everyone Should Know About." Forbes. 20 Jun. 2022.

[4] Doughty, Alison. "How the pharma industry is using digital twin technology." LinkedIn Pulse. 6 Jul. 2022.

[5] Fontecilla, Rod. "What Can Digital Twins Do for Healthcare?." Guidehouse Insights. 2 Jun. 2022.

[6] "How digital twins of human cells are accelerating drug discovery." Biopharma Dealmakers. ISSN 2730-6283.
[7] Kesari, Ganes. "Meet Your Digital Twin: The Coming Revolution In Drug Development." Forbes. 29 Sep. 2021.
[8] Patel, Sailesh K. "R&D Using the Metaverse and Digital Twins." Applied Clinical Trials. 1 Aug. 2022.
[9] Thomas, John. "The digital twin movement in pharma." Pharma Manufacturing. 22 Nov. 2021.
[10] Thilmany, Jean. "Bringing digital twins to boost pharmaceutical manufacturing." Venture Beat. 26 May 2022.
[11] Macdonald, Gareth John. "Digital Twins and AI Reshape Biopharmaceutical Manufacturing." Eng. News. 9 Aug. 2022.
[12] Poulsen, Leif. "How to benefit from digital twins in pharma manufacturing." NNE Tech Talk. Accessed 15 Feb. 2023.
[13] Chen, Yingjie et al. "Digital Twins in Pharmaceutical and Biopharmaceutical Manufacturing: A Literature Review." 8: 1088 (2020).
[14] Kansteiner, Fraiser. "After triumphant pilot, GSK eyes 'digital twins' to fine-tune vaccine production, development." Fierce Pharma. 23 Jun. 2021.
[15] Kansteiner, Fraiser. "Sanofi harnesses Dassault's digital twin tech to optimize production at future vaccine plants." Fierce Pharma. 26 Oct. 2022.
[16] Translational Systems Biology and In Silico Trials
Volume 2 - 2022
| https://doi.org/10.3389/fsysb.2022.928387
[17] An, G. (2022). Specialty Grand Challenge: What it Will Take to Cross the Valley of Death: Translational Systems Biology,"True" Precision Medicine, Medical Digital Twins, Artificial Intelligence And In Silico Clinical Trials. Front. Syst. Biol. 2, 5. doi:10.3389/fsysb.2022.901159
CrossRef Full Text | Google Scholar
[18] An, G. (2018). The Crisis of Reproducibility, the Denominator Problem and the Scientific Role of Multi-Scale Modeling. Bull. Math. Biol. 80 (12), 3071–3080. doi:10.1007/s11538-018-0497-0
PubMed Abstract | CrossRef Full Text | Google Scholar